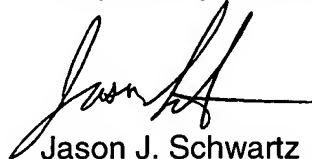


1-6 and 11-16 have been amended, claims 7-10 have been cancelled and new claims 17-23 have been added. The purpose of these amendments are to place the claims in a proper format for prosecution in the United States. No new matter has been added by these amendments.

Entry of this amendment and favorable examination of the application are respectfully requested.

Respectfully submitted,



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APPENDIX 1

Please cancel claims 7-10, enter new claims 17-23 and amend claims 1-6 and 11-16 as follows:

A1
1. (Amended) An isolated nucleic acid sequence encoding soluble nephrin or soluble nephrin-like molecules shared by pancreas and kidney glomerulus, comprising the nucleic acid sequence set forth in SEQ ID NO:1 or nucleic acid sequences having substantial similarity thereto and encoding nephrin-like molecules having the properties and functions characteristic of nephrin-like molecules, said nephrin-like molecules having an amino acid sequence substantially homologous with the amino acid sequence set forth in SEQ ID NO:2 lacking the amino acid sequence encoding the transmembraneous domain set forth in SEQ ID NO:3 of nephrin.

2. (Amended) The isolated nucleic acid sequence according to claim 1, wherein said amino acid sequence set forth in SEQ ID NO:2 has intracellular domains and extracellular domains, said nephrin-like molecules further comprising at least one contiguous amino acid sequence SEQ ID NO:4, said amino acid sequence set forth in SEQ ID NO:4 having intracellular and extracellular domains of SEQ ID NO:2.

3. (Amended) The isolated nucleic acid sequence according to claim 1, wherein said nucleic acid sequence further comprises a continuous nucleotide sequence set forth in SEQ ID NO:5, SEQ ID NO:6 or SEQ ID NO:7 derivable from a human nephrin encoding nucleic acid sequence set forth in SEQ ID NO:1.

Sub B14
4. (Amended) Soluble nephrin-like molecules shared by pancreas and kidney glomerulus, comprising polypeptides or derivatives thereof having the properties and functions characteristic of nephrin-like molecules and having an amino acid sequence substantially homologous with the amino acid sequence set forth in SEQ ID NO:2 lacking the transmembraneous domain set forth in SEQ ID NO:3 of nephrin.

5. (Amended) The soluble nephrin-like molecules according to claim 4, wherein said molecules further comprise at least one contiguous amino acid sequence substantially homologous to the amino acid sequence set forth in SEQ ID NO:4.

A1
cont'd
SUB
B15

6. (Amended) A binding substance, comprising an antibody which is capable of specifically recognizing and binding to a portion of an amino acid sequence overlapping an intracellular and extracellular domain of the soluble nephrin-like molecules according to claims 4 or 5 or to a portion of an amino acid sequence overlapping an intracellular and extracellular domain of the nucleic acid sequences encoding said soluble nephrin-like molecules.

A2
SUB
B16

11. (Amended) A method for diagnosing whether a subject suffers from nephropathies, inflammatory diseases, or neoplastic pancreatic diseases, said method comprising the steps of:

- (a) obtaining a blood or urine sample from a subject suspected of suffering from said diseases or being treated for said diseases;
- (b) contacting said sample with a reagent comprising soluble nephrin-like molecules according to claim 3; and
- (c) recording the absence or presence of a reaction of said soluble nephrin-like molecules when contacted with the sample.

12. (Amended) A method for evaluating the efficacy of treatment modalities in subjects suffering from nephropathies, inflammatory diseases or neoplastic pancreatic diseases, said method comprising the steps of:

- (a) obtaining a blood or urine sample from a subject suspected of suffering from said diseases or being treated for said diseases;
- (b) contacting said sample with a reagent comprising soluble nephrin-like molecules according to claim 3; and
- (c) recording the absence or presence of a reaction of said soluble nephrin-like molecules when contacted with the sample.

13. (Amended) A method for screening for the susceptibility of a population to nephropathies, inflammatory diseases or neoplastic pancreatic diseases, said method comprising the steps of:

- A2
cont'd
- (a) obtaining a blood or urine sample from a subject suspected of suffering from said diseases or being treated for said diseases;
 - (b) contacting said sample with a reagent comprising soluble nephrin-like molecules according to claim 3; and
 - (c) recording the absence or presence of a reaction of said soluble nephrin-like molecules and the autoantibodies present in the sample.

14. (Amended) A method for diagnosing whether a subject suffers from nephropathies, inflammatory diseases or neoplastic pancreatic diseases, said method comprising the steps of:

- SUB
B/L6 cont'd
- (a) obtaining a blood or urine sample from a subject suspected of suffering from said diseases or being treated for said diseases;
 - (b) contacting said sample with a reagent comprising a binding substance specifically recognizing and binding to a soluble nephrin-like molecule according to claim 3; and
 - (c) recording the absence or presence of a reaction when said binding substance is contacted with the sample.

15. (Amended) A method for evaluating the efficacy of treatment modalities in subjects suffering from nephropathies, inflammatory diseases or neoplastic pancreatic diseases, said method comprising the steps of:

- (a) obtaining a blood or urine sample from a subject suspected of suffering from said diseases or being treated for said diseases;
- (b) contacting said sample with a reagent comprising a binding substance specifically recognizing soluble nephrin-like molecules according to claim 3; and
- (c) recording the absence or presence of a reaction when contacting the binding substance with the sample.

16. (Amended) A method for screening the susceptibility of a population to nephropathies, inflammatory diseases or neoplastic pancreatic diseases, said method comprising the steps of:

- AA
Control
Sub
Bile acid
- (a) obtaining a blood or urine sample from a subject suspected of suffering from said diseases or being treated for said diseases;
- (b) contacting said sample with a reagent comprising a binding substance specifically recognizing a soluble nephrin-like molecule according to claim 3; and
- (c) recording the absence or presence of a reaction when contacting said binding substance with the sample.

Please enter new claims 17-23 as follows:

- A3
17. (New) The method according to claim 11, wherein said nephropathies comprise diabetic nephropathies and said inflammatory diseases comprise diabetes mellitus.
18. (New) The method according to claim 12, wherein said nephropathies comprise diabetic nephropathies and said inflammatory diseases comprise diabetes mellitus.
19. (New) The method according to claim 13, wherein said nephropathies comprise diabetic nephropathies and said inflammatory diseases comprise diabetes mellitus.
20. (New) The method according to claim 14, wherein said nephropathies comprise diabetic nephropathies and said inflammatory diseases comprise diabetes mellitus.
21. (New) The method according to claim 15, wherein said nephropathies comprise diabetic nephropathies and said inflammatory diseases comprise diabetes mellitus.
22. (New) The method according to claim 16, wherein said nephropathies comprise diabetic nephropathies and said inflammatory diseases comprise diabetes mellitus.
23. (New) A method for treating a patient with a nephropathy, an inflammatory disease or a neoplastic pancreatic disease, comprising administering to said patient a nucleic acid sequence according to claim 1.

APPENDIX 2

Please cancel claims 7-10 and amend claims 1-6 and 11-16 as follows:

1. (Amended) An isolated nucleic acid sequence encoding [a] soluble nephrin or soluble nephrin-like molecules shared by pancreas and kidney glomerulus, [c h a r a c t e r i z e d in that it comprises] comprising the nucleic acid sequence set forth in SEQ ID NO:1: or nucleic acid sequences [with] having substantial similarity thereto and encoding nephrin-like molecules [or derivatives thereof,] having the properties and functions characteristic of nephrin-like molecules, said nephrin-like molecules or derivatives thereof having an amino acid sequence substantially homologous with the amino acid sequence set forth in SEQ ID NO:2[: but] lacking the transmembraneous domain set forth in SEQ ID NO:3[:] of nephrin.
2. (Amended) The isolated nucleic acid sequence according to claim 1, [c h a r a c t e r i z e d in that it comprises the nucleic acid sequence SEQ ID NO:1: or nucleic acid sequences with substantial similarity encoding nephrin-like molecules or derivatives thereof, having the properties and functions characteristical of nephrin-like molecules,] wherein said amino acid sequence set forth in SEQ ID NO:2 has intracellular domains and extracellular domains, said nephrin-like molecules further comprising [having an amino acid sequence substantially homologous with SEQ ID NO:2: but lacking the transmembraneous domain SEQ ID NO:3: and having] at least one contiguous amino acid sequence set forth in SEQ ID NO:4 [(SEQ ID NO:4:)] having intracellular and [consisting of intra- and -]extracellular domains of SEQ ID NO:2[: or variations thereof].
3. (Amended) The isolated nucleic acid sequence according to claim 1, [c h a r a c t e r i z e d in that it comprises] wherein said nucleic acid sequence further comprises a continuous nucleotide sequence set forth in SEQ ID NO:5[:], SEQ ID NO:6[:] or SEQ ID NO:7[:] derivable from [the] a human nephrin encoding nucleic acid sequence set forth in SEQ ID NO:1[:].
4. (Amended) Soluble nephrin-like molecules shared by pancreas and kidney glomerulus, [c h a r a c t e r i z e d in that they comprise] comprising polypeptides [or derivatives thereof,] having the properties and functions characteristic[al] of nephrin-like

molecules and [being] having an amino acid sequence substantially homologous with the amino acid sequence set forth in SEQ ID NO:2[: but] lacking the transmembraneous domain set forth in SEQ ID NO:3[:] of nephrin.

5. (Amended) The soluble nephrin-like molecules according to claim 4, [c h a r a c t e r i z e d in that they] wherein said molecules further comprise at least one contiguous amino acid sequence substantially homologous to the amino acid sequence set forth in SEQ ID NO:4 [(SEQ ID NO:4:) or variations thereof].

6. (Amended) A binding substance, [c h a r a c t e r i z e d in that the binding substance is an antibody,] comprising an antibody which is capable of specifically recognizing and binding to a portion of an amino acid sequence overlapping an [the intra-] intracellular and extracellular domain of the soluble nephrin-like molecules according to claims [4-5] 4 or 5 or to a portion of an amino acid sequence overlapping [intra-] an intracellular and extracellular domain of the nucleic acid sequences encoding said soluble nephrin-like molecules.

11. (Amended) A method for diagnosing whether a subject suffers from [diabetic and other] nephropathies, [diabetes mellitus and other] inflammatory diseases, or neoplastic pancreatic diseases, said method comprising the steps of:

(a) obtaining a blood or urine sample from a subject suspected of suffering from said diseases or being treated for said diseases;

(b) contacting said sample with a reagent comprising soluble nephrin-like molecules according to claim 3 [or parts thereof]; and

(c) recording the absence or presence of a reaction of said soluble nephrin-like molecules when contacted with the sample.

12. (Amended) A method for evaluating the efficacy of treatment modalities in subjects suffering from [diabetic and other] nephropathies, [diabetes mellitus, and other] inflammatory diseases or neoplastic pancreatic diseases, said method comprising the steps of:

- (a) obtaining a blood or urine sample from a subject suspected of suffering from said diseases or being treated for said diseases;
- (b) contacting said sample with a reagent comprising soluble nephrin-like molecules according to claim 3 [or parts thereof]; and
- (c) recording the absence or presence of a reaction of said soluble nephrin-like molecules when contacted with the sample.

13. (Amended) A method for screening for the susceptibility of a population to [diabetic and other] nephropathies, [diabetes mellitus and other] inflammatory diseases or neoplastic pancreatic diseases [in large population groups], said method comprising the steps of:

- (a) obtaining a blood or urine sample from a subject suspected of suffering from said diseases or being treated for said diseases;
- (b) contacting said sample with a reagent comprising soluble nephrin-like molecules according to claim 3 [or parts thereof]; and
- (c) recording the absence or presence of a reaction of said soluble nephrin-like molecules and the autoantibodies present in the sample.

14. (Amended) A method for diagnosing whether a subject suffers from [diabetic and other] nephropathies, [diabetes mellitus and other] inflammatory diseases or neoplastic pancreatic diseases, said method comprising the steps of:

- (a) obtaining a blood or urine sample from a subject suspected of suffering from said diseases or being treated for said diseases;
- (b) contacting said sample with a reagent comprising a binding substance specifically recognizing and binding to a soluble nephrin-like molecule according to claim 3 [or parts thereof]; and
- (c) recording the absence or presence of a reaction when said binding substance is contacted with the sample.

15. (Amended) A method for evaluating the efficacy of treatment modalities in subjects suffering from [diabetic and other] nephropathies, [diabetes mellitus and other]

inflammatory diseases or neoplastic pancreatic diseases, said method comprising the steps of:

- (a) obtaining a blood or urine sample from a subject suspected of suffering from said diseases or being treated for said diseases;
- (b) contacting said sample with a reagent comprising a binding substance specifically recognizing soluble nephrin-like molecules according to claim 3 [or parts thereof]; and
- (c) recording the absence or presence of a reaction when contacting the binding substance with the sample.

16. (Amended) A method for screening the susceptibility of a population to [diabetic and other] nephropathies, [diabetes mellitus and other] inflammatory diseases or neoplastic pancreatic diseases, [in large population groups comprising] said method comprising the steps of:

- (a) obtaining a blood or urine sample from a subject suspected of suffering from said diseases or being treated for said diseases;
- (b) contacting said sample with a reagent comprising a binding substance specifically recognizing a soluble nephrin-like molecule according to claim 3 [or parts thereof]; and
- (c) recording the absence or presence of a reaction when contacting said binding substance with the sample.